

In re Application of:

Barbas, III et al

Application No.: 09/500,700

Filed: February 9, 2000

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PATENT

Attorney Docket No.: SCRIP1160-4

Page 87, line 25, in the paragraph beginning with, "DnaseI Footprinting Analysis," after the sequence ending in, "...GCACG -3'," please insert --(SEQ ID NO: 59)--.

Page 87, line 27, in the paragraph beginning with, "DnaseI Footprinting Analysis," after the sequence ending in, "...AACGG -3'," please insert --(SEQ ID NO: 60)--.

Page 88, line 31, in the paragraph beginning with, "The six finger proteins..." after the sequence ending in, "...GGGCG-3'," please insert --(SEQ ID NO: 61)--.

Page 88, line 31, in the paragraph beginning with, "The six finger proteins..." after the sequence ending in, "...CGGGG-3'," please insert --(SEQ ID NO: 62)--.

### IN THE CLAIMS

Please cancel non-elected claims 6-15, 20-39 and 41 without prejudice.

Please enter the following rewritten claims:

CE2  
3.

(Amended) The variant of claim 2, which is a zinc finger-nucleotide binding polypeptide selected from the group consisting of Zif268 and TFIIIA.

40. (Amended) An isolated zinc finger-nucleotide binding polypeptide variant produced by a method for isolating a zinc finger-nucleotide binding polypeptide variant which binds to a cellular nucleotide sequence comprising:

- C2
- a) identifying the amino acids in a zinc finger-nucleotide binding polypeptide that bind to a first cellular nucleotide sequence and modulate the function of the nucleotide sequence;
  - b) creating an expression library encoding the polypeptide variant containing randomized substitution of the amino acids identified in step a) above;
  - c) expressing the library in a suitable host cell; and
  - d) isolating a clone that produces a polypeptide variant that binds to a second cellular nucleotide sequence and modulates the function of the second nucleotide sequence,

wherein the variant is comprised of at least two zinc finger modules and wherein the amino acid sequence of at least one module that binds the second nucleotide sequence

C2  
Cane<sup>10</sup>  
comprises two cysteines and two histidines whereby both cysteines are amino proximal to both histidines and wherein at least one of the at least two modules of said variant has at least one amino acid sequence modification.

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Please add the following new claims:

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- Sub  
E4
- C3
- 42. (New) A hybrid zinc finger protein that binds to a target nucleic acid, the hybrid zinc finger comprising zinc fingers from a first protein linked to zinc fingers from a second protein.
43. (New) The hybrid zinc finger protein of claim 42, wherein at least two of the zinc fingers are variant zinc fingers.
44. (New) The hybrid zinc finger protein of claim 42, wherein the variant zinc fingers are mutagenized forms of natural zinc fingers.
45. (New) The hybrid zinc finger protein of claim 42 that modulates expression of the target nucleic acid.
46. (New) The hybrid zinc finger protein of claim 42, wherein the amino acid sequence of each zinc finger comprises two cysteines and two histidines whereby both cysteines are amino proximal to both histidines.
47. (New) A method for isolating a zinc finger protein that binds to a target nucleic acid, comprising:  
a) creating an expression library encoding variant zinc finger proteins, wherein the variant zinc finger proteins each comprises a plurality of zinc fingers, each zinc finger comprising two cysteines and two histidines whereby both cysteines are amino proximal to both histidines and an alpha helix is within the region bordered by the outermost cysteine and histidine residues, and the zinc finger proteins differ from each other in at